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REVIEW

Global Trends in Non-Invasive Techniques for the Diagnosis and Monitoring of Nonalcoholic Fatty Liver Disease: A Bibliometric and Visualization Analysis

Jing-Wen Cai[1,*], Wei-Long Wang[1,*], Dong-Ling Lin[2], Shu-Feng Ren[1], Qian-Qian Jia[1], Xiao-Xuan He[1], Xue-Xia Yang[1], Wen Cai[1], Hui Hou[3]

[1]Department of Nursing, Xinjiang Medical University, Urumqi, People's Republic of China; [2]Department of Infectious Diseases, First Affiliated Hospital of Xinjiang Medical University, Urumqi, People's Republic of China; [3]Department of Gastroenterology, Fifth Affiliated Hospital of Xinjiang Medical University, Urumqi, People's Republic of China

*These authors contributed equally to this work

Correspondence: Wen Cai, Department of Nursing, Xinjiang Medical University, Urumqi, People's Republic of China, Email caiwen820602@163.com; Hui Hou, Department of Gastroenterology, Fifth Affiliated Hospital of Xinjiang Medical University, Urumqi, People's Republic of China, Email 11547850@qq.com

Background: Nonalcoholic fatty liver disease (NAFLD) is a globally prevalent condition. Emerging technologies like biomarkers, imaging, multi-omics, and artificial intelligence (AI) are driving research into non-invasive diagnosis and monitoring.

Objective: To provide a comprehensive overview of the hotspots and future research trends in non-invasive diagnosis and monitoring of NAFLD.

Methods: A search of the Web of Science Core Collection database identified 1136 articles that met the study criteria between April 1, 2005, and December 31, 2024. By integrating various bibliometric methods and tools, we conducted a comprehensive analysis.

Results: Publication growth reflects robust research interest. The United States and China are the leading countries, and the University of California, San Diego tops the institutions. Liver International and PLOS ONE publish the most relevant articles, while Journal of Hepatology is the most influential. "Transient elastography", "fibrosis" and "diagnosis" are prominent keywords. Research trends are shifting from basic to clinical applications, with a focus on non-invasive techniques, biomarkers and disease models.

Conclusion: Future investigations will focus on the clinical application of these techniques. Global collaboration is expected to enhance NAFLD diagnosis, treatment, prevention, and monitoring.

Keywords: non-invasive techniques, nonalcoholic fatty liver disease, bibliometric analysis, visualization

Introduction

Nonalcoholic fatty liver disease (NAFLD) is one of the most common liver diseases worldwide and poses a significant threat to human health. NAFLD is defined as the presence of steatosis affecting more than 5% of hepatocytes without excessive alcohol consumption or other chronic liver diseases.[1,2] Its severity varies due to the injury and resulting fibrosis, potentially progressing to a more severe form of inflammation and hepatocyte damage known as non-alcoholic steatohepatitis (NASH). NASH is often accompanied by the progression of cellular fibrosis to cirrhosis, ultimately deteriorating into hepatocellular carcinoma.[3] In early 2020, an international panel of experts renamed NAFLD to "metabolic dysfunction-associated fatty liver disease" (MAFLD) using the Delphi consensus method.[4] In 2023, three major international hepatology associations proposed replacing the NAFLD with "metabolic dysfunction-associated steatotic liver disease" (MASLD).[5,6] The newly established nomenclature system for fatty liver disease provides a more appropriate name for this highly prevalent liver condition, emphasizing the concept of metabolic dysfunction underlying the disease. Currently, the prevalence of MASLD has reached

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38% among adults worldwide, posing a serious threat to human health.[7] In clinical practice, it's common to observe that patients with MAFLD exhibit a spectrum of intrahepatic injuries, including simple steatosis. Concurrently, substantial evidence clearly demonstrates that patients with NAFLD and MAFLD not only face increased risk of hepatic events but also have a higher risk of extrahepatic complications such as cardiovascular disease (CVD) and extrahepatic cancers. These risks increase the global public health burden and attract wide attention from researchers worldwide.[8,9]

Currently, in the clinical diagnosis of NAFLD, liver biopsy remains the "gold standard", but due to its invasive nature, it is not suitable for large-scale population screening.[10,11]

Therefore, many scholars have gradually shifted their focus to non-invasive diagnostic techniques and monitoring of NAFLD.[12] Non-invasive techniques primarily rely on serum biomarker levels and imaging technologies, with the two approaches complementing each other.[13] Jenny Lee et al,[14] through a literature review, have highlighted the significant efficacy of non-invasive fibrosis markers such as the NAFLD Fibrosis Score (NFS) and Fibrosis-4 (FIB-4) in aiding the diagnosis and exclusion of liver fibrosis. Moreover, NFS and FIB-4 can serve as prognostic markers to assess disease progression and outcomes. Transient elastography (TE) plays a crucial role in assessing the degree of liver steatosis and fibrosis, whereas magnetic resonance imaging (MRI) can precisely quantify liver fat content, providing high-resolution imaging information for disease diagnosis.[15,16] Among these, the controlled attenuation parameter (CAP) is measured using TE devices such as FibroScan.[17] The parameter reflects the extent of fat accumulation in the liver and is primarily used to assess the degree of hepatic steatosis. However, conventional MRI is not sensitive to mild steatosis. Research indicates that magnetic resonance spectroscopy (MRS) is the most accurate non-invasive technique for measuring liver fat content and has been widely used in several large-scale epidemiological studies.[18] In recent years, magnetic resonance imaging proton density fat fraction (MRI-PDFF) has emerged as a novel non-invasive diagnostic method for clinical assessment of liver fat content.[19] Compared with other techniques, MRI-PDFF can accurately and rapidly determine liver fat content, with high sensitivity and specificity, as well as good reproducibility and repeatability.[20] With the continuous advancement of omics technologies, illustrated in Figure 1, the integration of multi-omics for the diagnosis and monitoring of NAFLD is gradually being

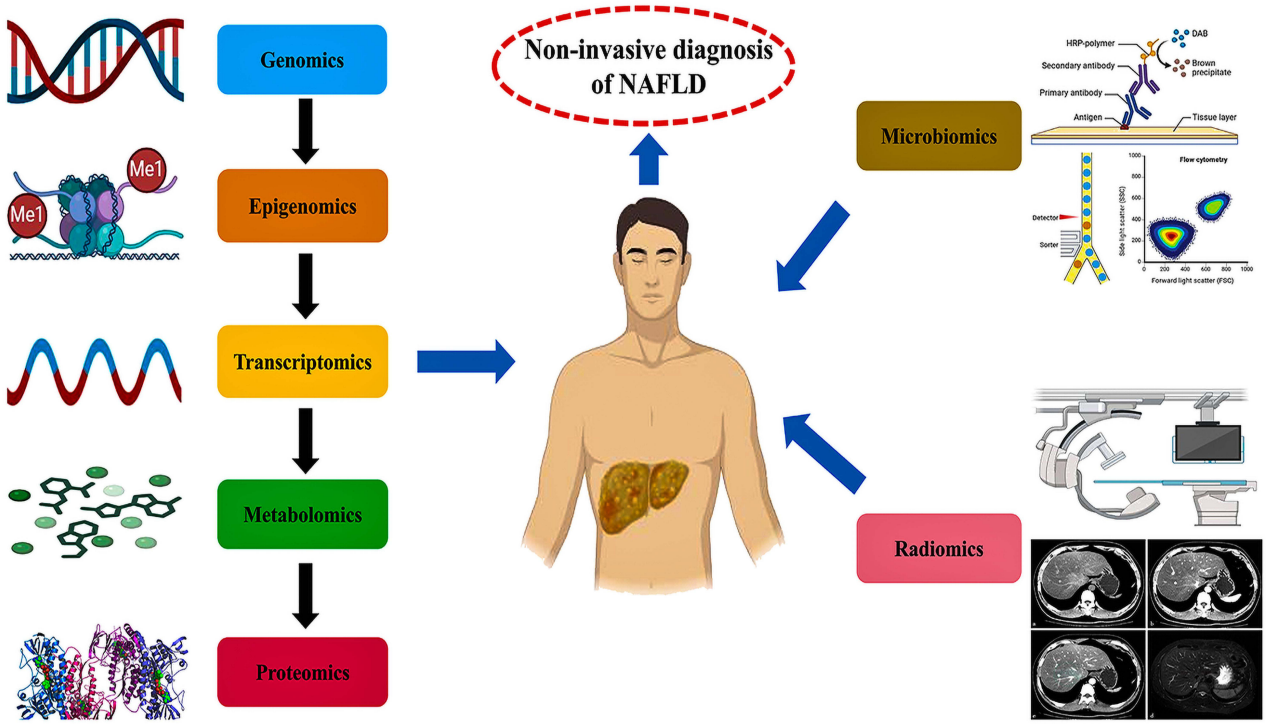

Figure 1 Application of multi-omics techniques for non-invasive diagnosis of NAFLD.

implemented in clinical practice.[21,22] The advent of the information age has spurred a series of innovations in computational science, and the rise of artificial-intelligence-assisted diagnostics is gradually emerging. The development and validation of NAFLD prediction models using machine learning or deep learning algorithms and the realization of personalized precision medicine will become the focus of future research.[23,24]

However, there are significant gaps in this field, including the lack of unified diagnostic thresholds across populations, isolated validation of individual techniques, the absence of combined diagnostic models, and artificial intelligence (AI) prediction models that predominantly rely on single-center retrospective data with low clinical translation rates.[25] Based on bibliometric analysis, this study aims to provide a new perspective for clinicians and relevant researchers, indicating the direction for future research.

Research Framework and Methods

Research Steps and Framework

The Web of Science core collection (WoSCC) database was used for the literature search and bibliometric analyses. The following search criteria were developed to ensure a thorough search: TS = ("non-invasive") and TS = ("non-alcoholic fatty liver" or "non-alcoholic steatohepatitis" or "NAFLD"). There were no restrictions on language or type of literature. The search was conducted from 1 April 2005 to 31 December 2024 and identified 1801 articles. After a rigorous screening process that excluded 303 review articles, 40 editorial materials, 257 conference abstracts, 36 letters, and 2 corrections, 1163 articles remained. Additionally, 27 non-English language articles were excluded, leaving 1136 articles for analysis. The detailed ranking process is shown in Figure 2.

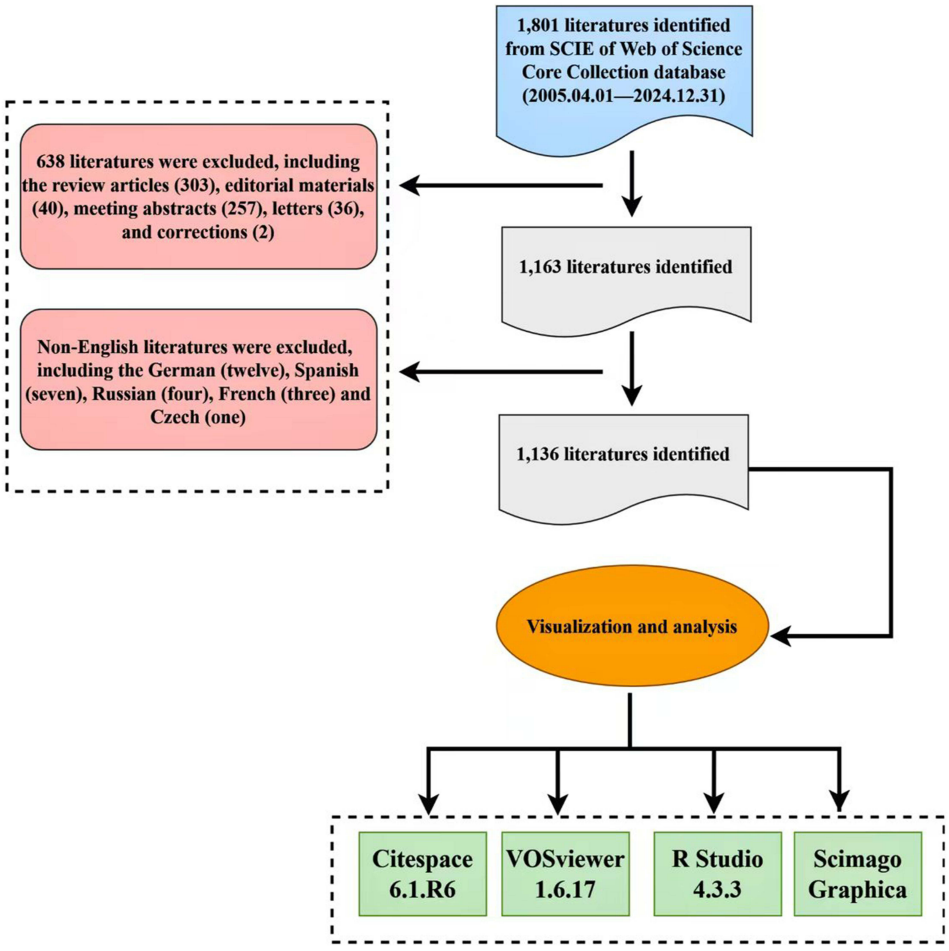

Figure 2 Screening process flowchart.

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Methods and Analysis

In this study, we utilized CiteSpace 6.1.R6 to conduct timeline analysis of keywords and dual-map overlay analysis of journals. VOSviewer 1.6.17 constructs network maps based on citation, bibliographic coupling, co-citation, or co-author relationships, analyzes the co-occurrence relationships of keywords in the literature, and helps identify research hotspots and trends.

The analysis of the conceptual structure in NAFLD research, visualization of global publication distribution, annual author output, keyword importance, and topic evolution was conducted using the "bibliometrix" package in RStudio (version 4.3.3). Scimago Graphica was utilized for the analysis of publication volumes by country and the total strength of collaboration network. Through the integration of various bibliometric tools and methods, we comprehensively analyzed the clinical efficacy of non-invasive techniques in the fields of NAFLD diagnosis and disease course monitoring, as well as their future development directions.

Results

Analysis of Publication Quantity

Based on the data collected, analysis of the annual publication numbers from 2005 to 2024 provided us with a visual means of quantitatively assessing the overall trends in the field of research related to non-invasive techniques for diagnosing and monitoring NAFLD.

As shown in Figure 3A, the number of papers published in related research areas gradually increased from 2 papers in 2005 to 124 papers in 2024, showing a steady upward trend in publications. From 2020 onwards, the number of publications has increased significantly, with more than 100 papers published annually, reaching its peak in 2023. This trend was further confirmed by the fitted curve in Figure 3B, with a coefficient of determination (R^2) of 0.9319, indicating a steady increase in the article output.

This trend also heralds the substantial potential of this field for future basic research and clinical applications.

Conceptual Structure Map Analysis of NAFLD Research Fields

Figure 4 presents a conceptual structure map that outlines various research areas associated with NAFLD. These findings indicate that the multidimensional correspondence analysis (MCA) method has effectively illustrated the connections and structural relationships among different medical concepts pertinent to the diagnosis and assessment of liver diseases. Each point in the diagram represents a unique medical concept, with the spatial distance between points indicating the level of conceptual similarity or association. Notably, the first two dimensions (Dim 1 and Dim 2) account for 28.55%

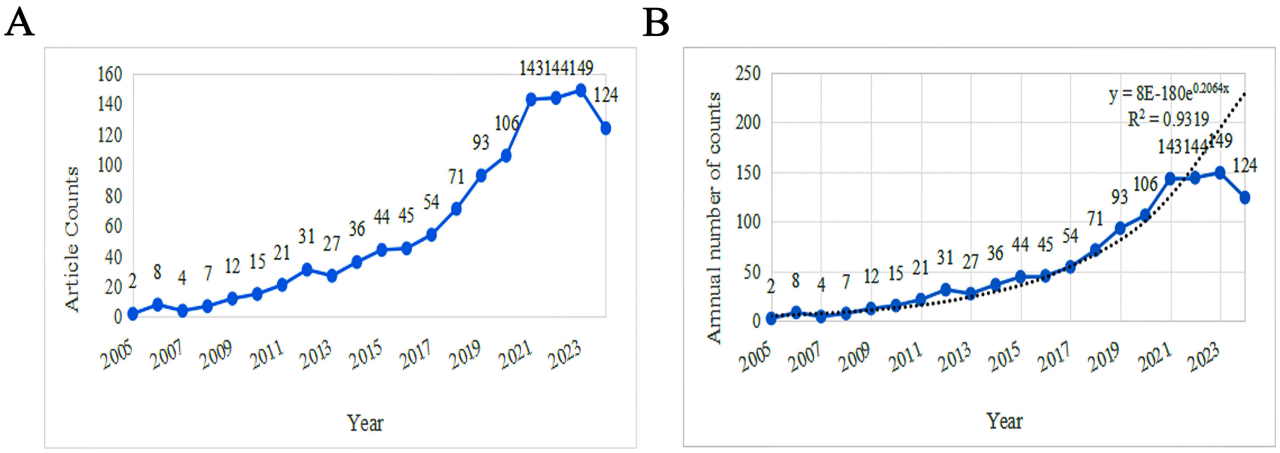

Figure 3 (**A**) Line graph of the number of research publications related to non-invasive techniques for the diagnosis and monitoring of NAFLD worldwide. (**B**) Fitted curve of global annual trends in the publication of studies related to non-invasive techniques for the diagnosis and monitoring of NAFLD (R^2 = 0.9319).

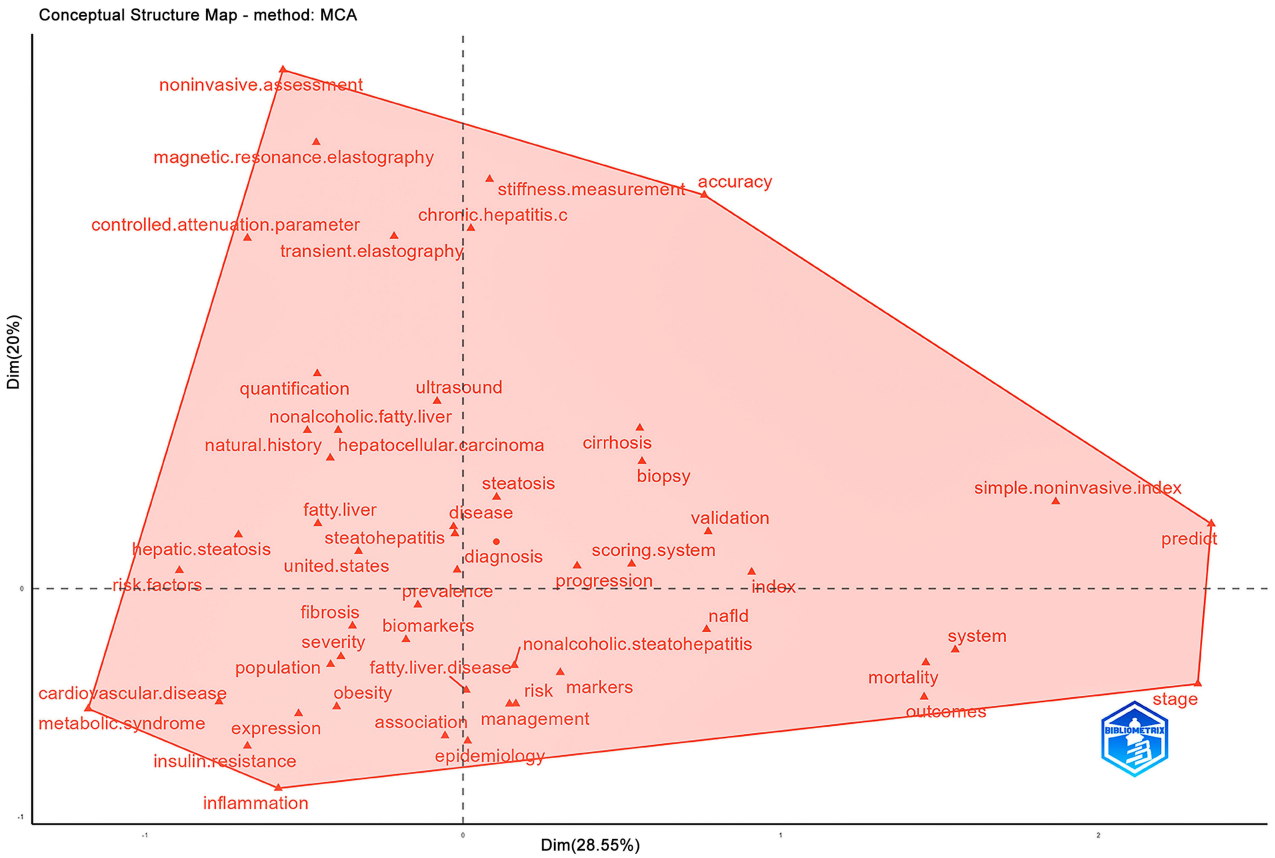

Figure 4 Conceptual structure map of NAFLD research fields. The triangles in the diagram represent different research directions, the double triangles represent major research areas, and the dots indicate specific research related to the topic.

and 9.94% of the overall variability, respectively, emphasizing the primary dimensions that distinguish these concepts within the field.

The figure illustrates a significant association between non-invasive evaluation techniques, including magnetic resonance elastography and transient elastography, and the diagnosis of liver disorders. The accuracy of diagnosing chronic hepatitis C is closely related to diagnostic precision and stiffness measurements. Quantification techniques and ultrasound are associated with the assessment of NAFLD and hepatocellular carcinoma, whereas cirrhosis and biopsy contribute to determining the severity of steatosis and steatohepatitis.

Furthermore, the strong correlation between non-invasive indices, their predictive capacities, validation, scoring systems, and diagnosis highlights the important role of these indices in both predicting and diagnosing liver disease. Pathophysiological mechanisms, such as obesity, metabolic syndrome, insulin resistance, and inflammation, are associated with risk, fibrosis, and severity. The relationships among NAFLD, biomarkers, systematic evaluations, mortality, and outcomes are linked to staging, cardiovascular disease, risk markers, management strategies, and epidemiological research, emphasizing the significance of these elements in the comprehensive evaluation of NAFLD. This conceptual framework reveals the global focus and direction of research in the area of non-invasive techniques for NAFLD, further illustrating global research trends.

Analysis of Countries and Publications

Research has revealed that scholars from China and the United States collectively produce significantly more publications than their counterparts from other countries, as illustrated in Figure 5A. Among these, American scholars led with the highest number of articles in the area of non-invasive techniques for the diagnosis and monitoring of NAFLD, totaling 224

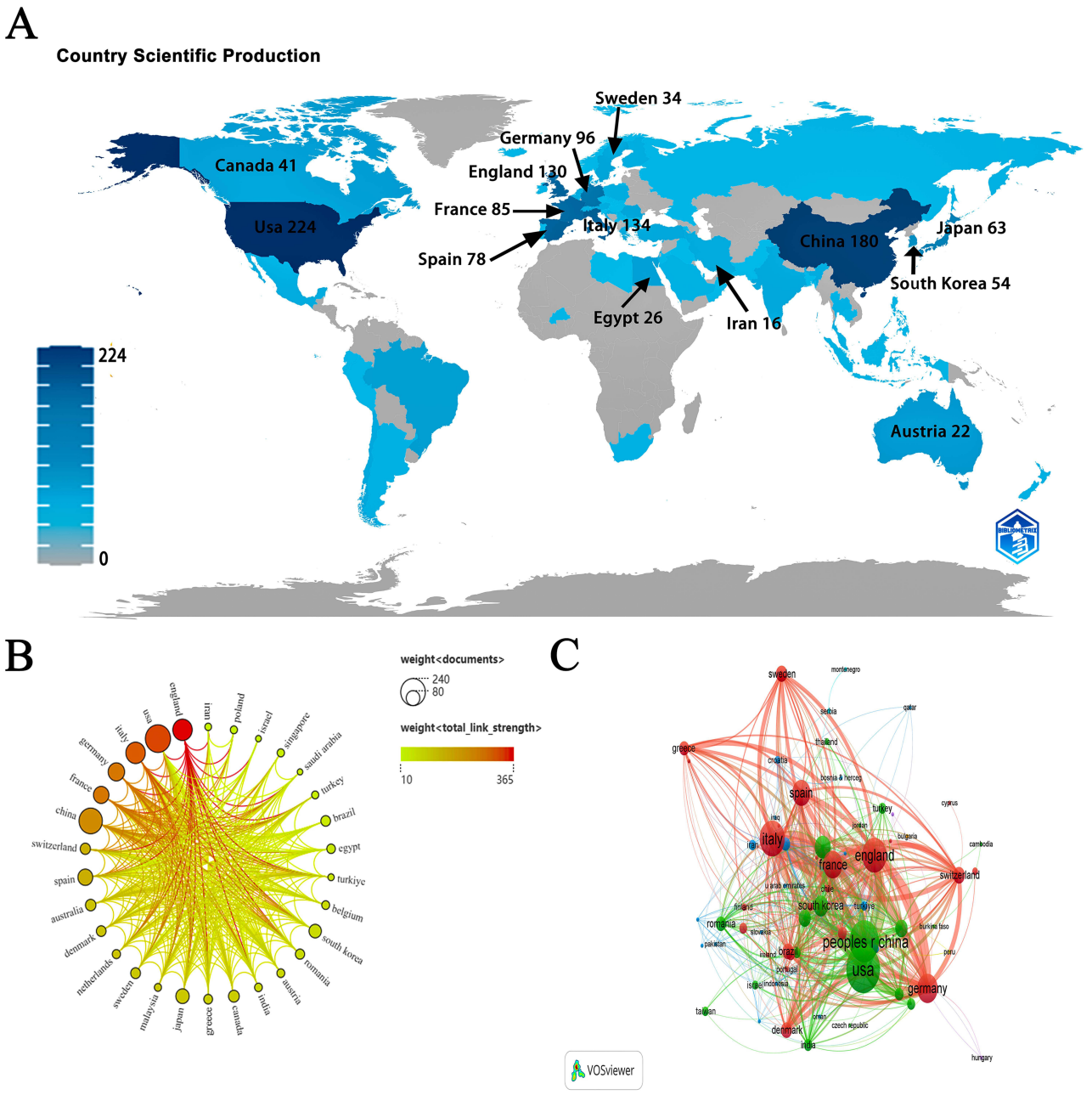

Figure 5 (**A**) A world map of the distribution of research publications related to non-invasive techniques for the diagnosis and monitoring of NAFLD. (**B**) Number of publications by country and total collaboration strength. (**C**) Countries/territories collaboration analysis by VOSviewer.

publications, which represents 19.72% of the global publication output. Close behind are Chinese scholars, who have contributed 180 publications, accounting for 15.85% of the total. Italy and England have also surpassed the 100-article mark, as detailed in Table 1. Additionally, when considering aspects of collaboration, Austria exhibits the centripetal indices of 0.43, while Germany and Iran have equal centripetal indices of 0.41, suggesting that these countries not only excel in the domain of non-invasive diagnostic techniques for NAFLD but also emphasize international cooperation significantly.

Figure 5B and C depict the international communication and collaborative efforts in this research field, with a particular focus on regions including North America, Western Europe, and East Asia. The United States and China have the highest number of collaborative publications, and they also have a high level of collaboration with other countries around the world, indicating that both countries have significant academic influence and activity in the field of research related to non-invasive diagnosis and monitoring of NAFLD.

Table 1 Top 10 Countries in Terms of Publications and Centrality

Rank	Documents	Centrality	Country	Rank	Centrality	Documents	Country
1	224	0.18	USA	1	0.43	22	Austria
2	180	0	China	2	0.41	96	Germany
3	134	0	Italy	3	0.41	16	Iran
4	130	0.04	England	4	0.33	1	Oman
5	96	0.41	Germany	5	0.32	34	Sweden
6	85	0	France	6	0.29	3	Qatar
7	78	0.07	Spain	7	0.28	18	Malaysia
8	63	0.12	Japan	8	0.28	3	Slovakia
9	54	0	South Korea	9	0.23	30	Romania
10	41	0.06	Canada	10	0.23	26	Egypt

Analysis of Institutional Publications

Regarding research output from various global institutions, Table 2 illustrates the top ten institutions worldwide based on their publication output. At the forefront is the University of California, San Diego, with 41 publications. Following closely are Newcastle University, Chinese University of Hong Kong, and Virginia Commonwealth University, with 33, 32, and 25 publications, respectively. The University of Oxford is also notable, contributing 23 publications.

In Figure 6A, a network diagram generated through VOSviewer software visually represents the co-authorship connections among diverse universities and research institutions. The nodes within the graph represent individual research institutions, with connecting lines symbolizing established the collaborative links in academic research. The various colors illustrate the types of collaboration among different institutions. Additionally, the size of the nodes corresponds to both the frequency of collaborations and the volume of published articles, whereas the thickness of the lines between nodes reflects the intensity of these collaborations.

The figure clearly indicates that collaboration among Chinese research institutions is primarily domestic, with limited partnerships with institutions in other countries. This situation somewhat constrains the academic perspectives of local researchers and scholars focusing on NAFLD-related subjects. As depicted in Figure 6B, which presents the average publication year for non-invasive diagnostic and monitoring techniques for NAFLD across global research institutions, the majority of findings are concentrated in China, the United States, England, Japan, and France. Recently, there has been a notable increase in the number of publications from domestic research entities in this field. Nevertheless, most inter-institutional collaborations have predominantly occurred at the national level, resulting in a deficiency of international academic exchanges and partnerships, which hampers the long-term progression of research efforts. Moving forward, it is imperative for research institutions worldwide to bolster cross-border collaborations and actively promote the translation of research findings into clinical applications within this domain.

Table 2 Top 10 Institutions with the Most Publications

Rank	Documents	Centrality	Institution	Country
1	41	0.14	Univ Calif San Diego	USA
2	33	0.18	Newcastle Univ	England
3	32	0.15	Chinese Univ Hong Kong	China
4	25	0.14	Virginia Commonwealth Univ	USA
5	23	0	Univ Oxford	England
6	21	0.23	Wenzhou Med Univ	China
7	18	0.01	Shanghai Jiao Tong Univ	China
8	18	0.32	Harvard Med Sch	USA
9	17	0.14	Yokohama City Univ	Japan
10	16	0	Sorbonne Univ	France

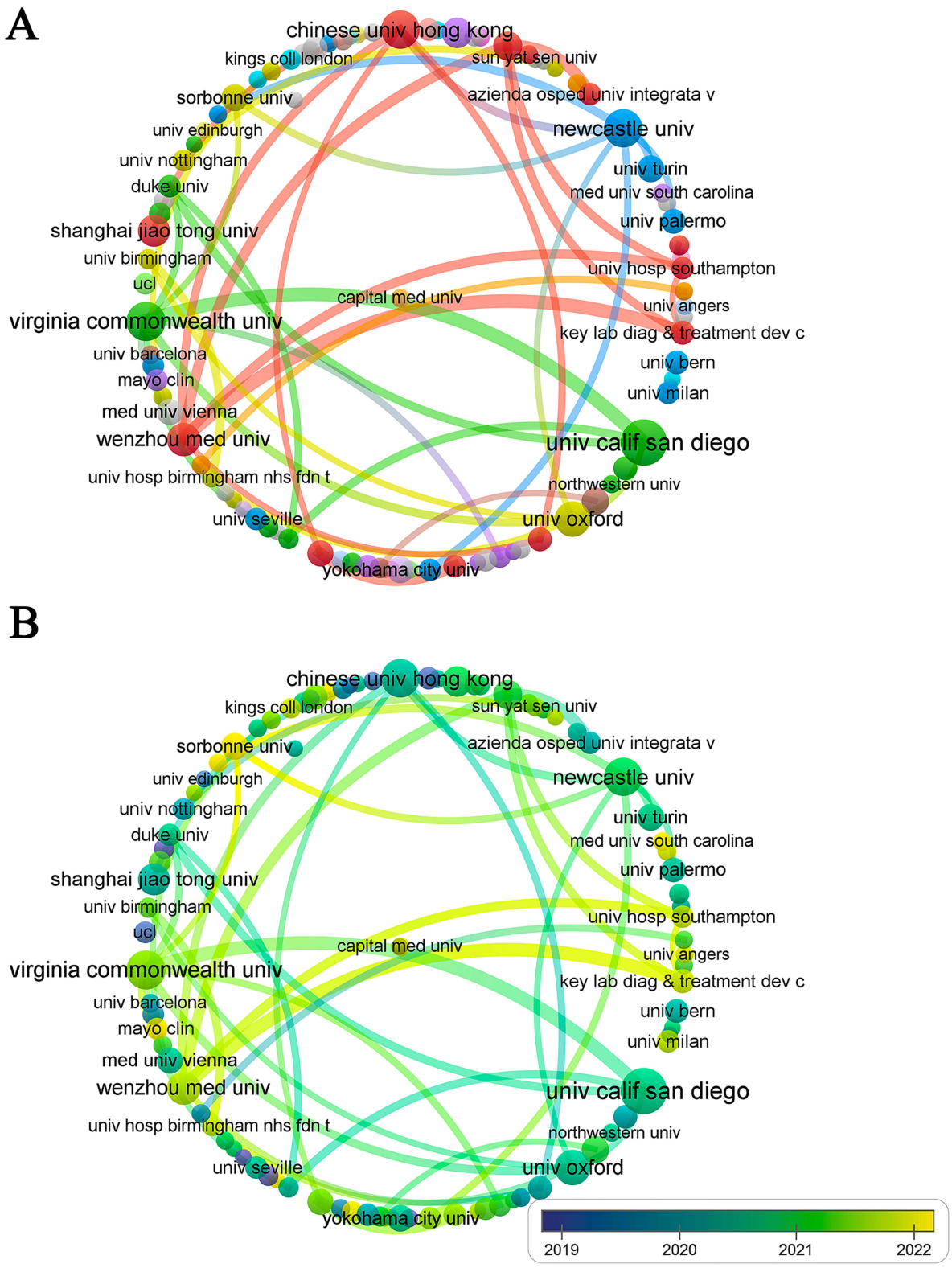

Figure 6 (**A**) VOSviewer network visualisation for institutional co-authorship analysis. (**B**) Average year of publication by institution in the field of non-invasive techniques for diagnosis and monitoring of NAFLD.

Analysis of the Most Influential Journals

An analysis of research articles dedicated to non-invasive techniques for the diagnosis and monitoring of NAFLD revealed a substantial output of 308 publications within this research field. These articles were published across approximately 44 different journals, each contributing at least five papers to scholarly literature. Table 3 presents a comprehensive analysis, showing the top ten journals in this field along with the corresponding number of published articles, total citations, and journal impact factor for the year 2024. Notably, Liver International stands out as the leading journal with a remarkable total of 57 relevant publications, closely followed by PLOS ONE with 45 articles. In terms of influence, the Journal of Hepatology emerged as the most influential, with the highest citation count of 6255 and an impressive impact factor of 26.8, indicating widespread recognition and frequent referencing within the academic community. Furthermore, Figure 7A illustrates the average publication year for each journal, indicating that Liver International holds a significant concentration of articles authored by early career researchers. Figure 7B provides a macroscopic view of the evolving cumulative publication counts across various journals from 2005 to the present. The visual representation clearly illustrates a consistent upward trend in the number of publications across all journals. Notably, the Journal of Hepatology and Liver International has emerged as the top two journals in terms of publication volume and growth rate. Conversely, Alimentary Pharmacology & Therapeutics and PLOS ONE exhibit a slower growth pace. Remarkably, Scientific Reports, despite its later inception in 2011, demonstrates rapid growth. These journals have promoted the development of research fields related to NAFLD through their significant academic influence.

In Figure 7C, a map overlay of journals is depicted, with citing journals positioned on the left and cited journals on the right. The primary citation pathway is denoted by the green line. Analysis of the figure reveals that citing journals are linked to publications in the fields of medicine, pharmacy, and clinical studies, whereas the cited journals are associated with molecular/biology/genetics ($z = 4.55$, $f = 3360$), and health/nursing/and medicine ($z = 6.36$, $f = 4633$), respectively.

Analysis of the Most Influential Authors

The top ten most influential researchers are listed in Table 4. Among them, Loomba, Rohit's team from the University of California, San Diego, ranked first with a total of 31 publications; the number of citations for a per paper was 94.87, second only to Harrison, Stephen A.'s team from the University of Oxford, which had 109.50 citations for a per paper, and Targher et al's team from Italy, which ranked second in terms of the number of publications. The second highest number of publications was by Prof. Targher, Giovanni's team from Italy, with 23 research papers in NAFLD-related fields as of 2024. They were followed by Zheng and Ming-Hua's team from Shanghai Jiao Tong University, with 21 papers. Figure 8A illustrates the co-occurrence analysis of researchers, with brighter nodes indicating a higher frequency of occurrence. A minimum criterion of at least six publications for each author was established, revealing that the research teams or laboratories of Loomba, Rohit, Targher, Giovanni, Bugianesi, and Elisabetta worked closely in the research field, focusing on non-invasive diagnosis and monitoring of NAFLD. Additionally, the majority of collaborations among these authors occurred primarily within their countries.

Table 3 Top 10 Journals in Terms of Publications and Citations

Rank	Source	Documents	Citations	IF (2024)
1	Liver International	57	2243	6.00
2	PLOS ONE	45	1166	2.90
3	Journal of Hepatology	43	6255	26.80
4	Scientific Reports	39	696	3.80
5	Alimentary Pharmacology & Therapeutics	37	1464	6.60
6	Obesity Surgery	25	377	2.90
7	JHEP Reports	24	383	9.50
8	Journal of Clinical Medicine	23	190	3.00
9	World Journal of Gastroenterology	19	1118	4.30
10	Diagnostics	17	195	3.00

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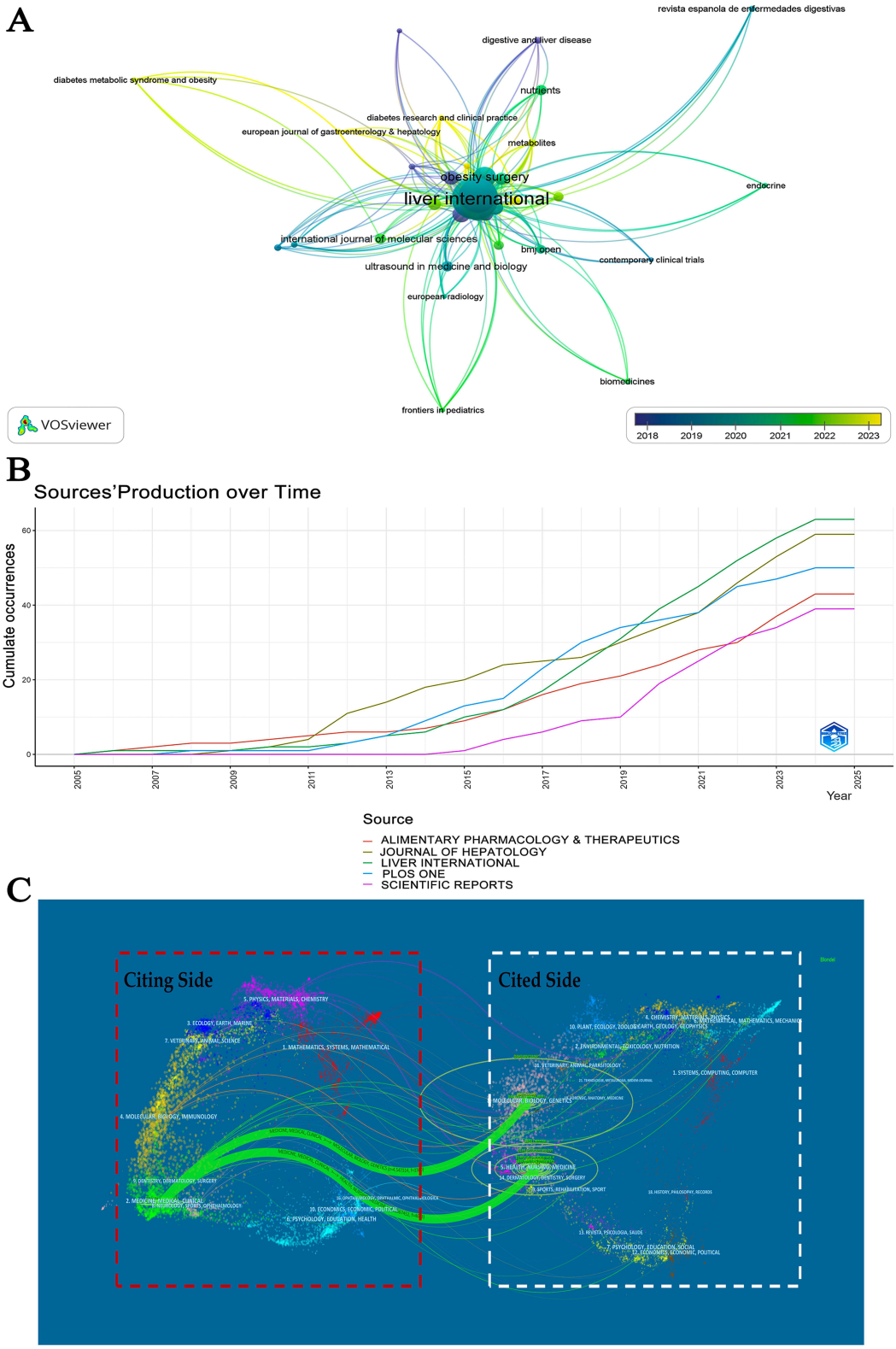


Figure 7 (**A**) Average year of publication in the field of non-invasive techniques for diagnosis and monitoring of NAFLD by journal. (**B**) Journal' production over time. (**C**) The dual-map overlays of journals.

Table 4 Top 10 the Most Productive Authors Distributed by Publications and Citations

Rank	Author	Documents	Citations	Link Strength	Average Citation
1	Loomba, Rohit	31	2941	566	94.87
2	Targher, Giovanni	23	400	394	17.39
3	Zheng, Ming-Hua	21	822	530	39.14
4	Wong, Vincent Wai-Sun	20	1246	677	62.30
5	Anstee, Quentin M.	20	1798	676	89.90
6	Sanyal, Arun J.	20	816	349	40.80
7	Boursier, Jerome	19	1403	590	73.84
8	Bugianesi, Elisabetta	18	1265	501	72.28
9	Ratziu, Vlad	17	1314	540	77.29
10	Harrison, Stephen A.	16	1752	478	109.50

The results indicate that the authors analyzed all have a positive scientific output between 2006 and 2024. Figure 8B illustrates the number of publications and the total annual citations per author over time. Wong, Vincent Wai-Sun, and Loomba, Rohit maintained a robust scholarly output and high citation frequency throughout the observation period, reflecting their continued influence in the field. Ratziu, Vlad, Anstee, Quentin M., Bugianesi, Elisabetta, Boursier, Jerome, Targher, Giovanni, Zheng, Ming-Hua, and other authors gradually increased their scientific output after 2012, especially after 2018, when their publication volume and citation frequency increased significantly, showing strong research activity and influence growth.

Analysis of Citation and Co-Citation

CiteSpace was employed to examine and visualize the 25 documents with the most intense citation bursts, as shown in Figure 9A, which illustrates the duration of these bursts for the references. Notably, Angulo, P's 2015 publication in Gastroenterology titled "Liver Fibrosis, but No Other Histologic Features, Is Associated With Long-term Outcomes of Patients With Nonalcoholic Fatty Liver Disease" recorded the highest citation burst intensity at 32.96, indicating frequent citations from 2016 to 2020. Furthermore, we present a list of the ten most frequently cited literatures in Table 5. At the top of this list is "Design and validation of a histological scoring system for nonalcoholic fatty liver disease" led by Kleiner et al, published in Hepatology in 2005, which garnered 340 citations. Following closely is "NAFLD fibrosis score: A noninvasive system that identifies liver fibrosis in patients with NAFLD" with an overall citation count of 265. In Figure 9B, articles with over 25 citations within the realm of non-invasive diagnostic and monitoring techniques for NAFLD are displayed, while Figure 9C highlights the most influential research papers based on co-citation analysis conducted with VOSviewer.

Frequency and Centrality of Keywords

As shown in Table 6, we conducted a comprehensive analysis of the top ten keywords associated with non-invasive techniques for the diagnosis and monitoring of NAFLD. Among these, the terms "fibrosis", "nafld", and "diagnosis" demonstrated high frequency. Furthermore, keywords such as "health", "noninvasive assessment", and "cardiovascular disease" exhibited strong centrality, indicating these keywords have dense connections with other keywords. By evaluating both the frequency and centrality of these keywords, we can identify current research priorities and emerging trends.

Burst Analysis of Keywords

By employing the Citespace algorithm, we conducted an analysis of keyword bursts to track the evolving research trends in the field. Figure 10 presents the 25 keywords that exhibited the most significant citation outbreaks. Among these, "transient elastography" emerged with the highest burst intensity (8.76), closely followed by "chronic hepatitis C" (6.81). Notably, the keyword "follow up" exhibited the longest burst duration, spanning five years from 2015 to 2020. Recently, notable keywords with high citation rates have included "non-invasive tests" (2022–2024), "nash" (2022–2024), and "liver" (2022–2024). The

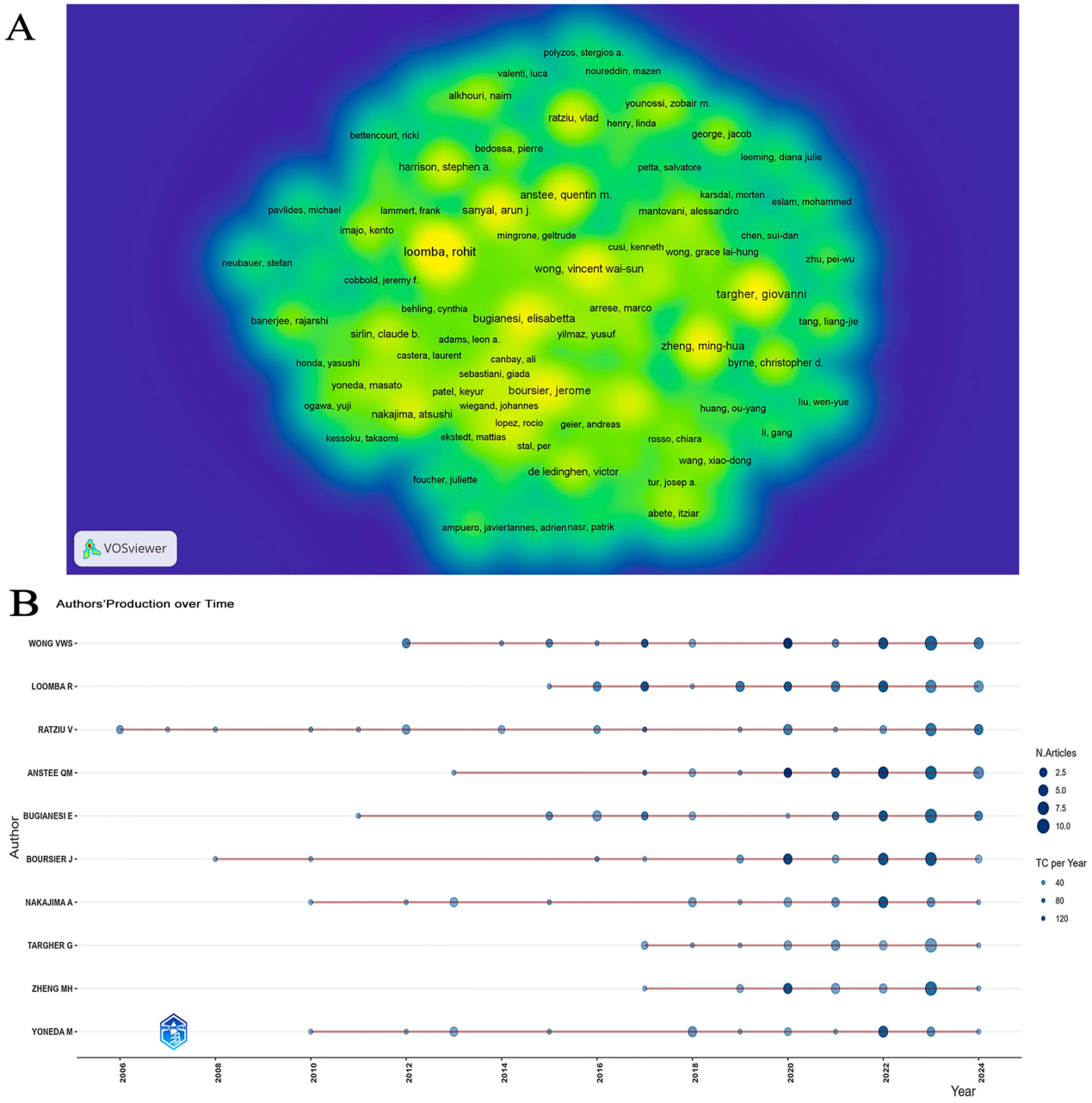


Figure 8 (**A**) A co-occurrence analysis of researchers with a threshold of at least six publications per author. (**B**) Authors' production over time.

emergence of new burst keywords and the frequency of notable bursts in recent years have contributed to rapid advancements in this field.

Cloud Analysis of Keywords

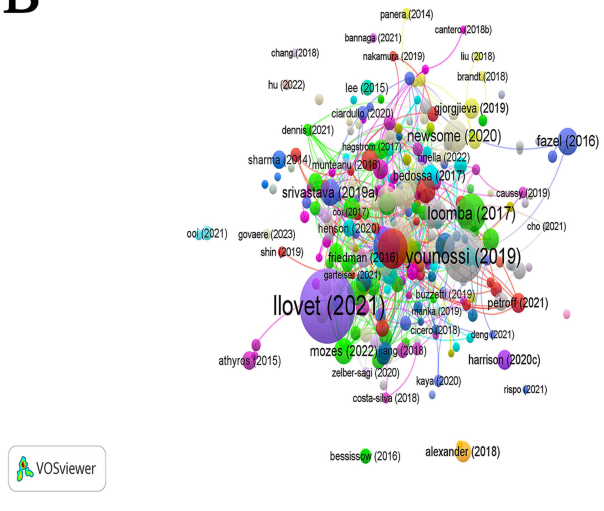
In this study, the assessment utilized the "bibliometrix" package to visually highlight key terms relevant to NAFLD research by varying text size and color. As depicted in Figure 11A, the term "fibrosis" was presented in the largest font size, emphasizing its critical role in liver disease progression and its association with NAFLD and NASH development. Furthermore, several non-invasive diagnostic techniques, such as ultrasound and transient elastography, are widely employed for the clinical evaluation and monitoring of NAFLD. Such investigative efforts are essential for setting research priorities and guiding clinical practices in NAFLD management, ultimately improving patient outcomes and advancing the field.

A

Top 25 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	2005 - 2024
Chalasani N, 2012, HEPATOLOGY, V55, P2005, DOI 10.1002/hep.25762, DOI	2012	23.3	2014	2017	
Vernon G, 2011, ALIMENT PHARM THER, V34, P274, DOI 10.1111/j.1365-2036.2011.04724.x, DOI	2011	11.88	2014	2016	
Chalasani N, 2012, GASTROENTEROLOGY, V142, P1592, DOI 10.1053/j.gastro.2012.04.001, DOI	2012	11.01	2014	2017	
Musso G, 2011, ANN MED, V43, P617, DOI 10.3109/07853890.2010.518623, DOI	2011	8.89	2014	2016	
Angulo P, 2013, GASTROENTEROLOGY, V145, P782, DOI 10.1053/j.gastro.2013.06.057, DOI	2013	7.97	2014	2018	
Kwok R, 2014, ALIMENT PHARM THER, V39, P254, DOI 10.1111/apt.12569, DOI	2014	11.3	2015	2019	
Williams CD, 2011, GASTROENTEROLOGY, V140, P124, DOI 10.1053/j.gastro.2010.09.038, DOI	2011	10.39	2015	2016	
Angulo P, 2015, GASTROENTEROLOGY, V149, P389, DOI 10.1053/j.gastro.2015.04.043, DOI	2015	32.96	2016	2020	
Ekstedt M, 2015, HEPATOLOGY, V61, P1547, DOI 10.1002/hep.27368, DOI	2015	19.87	2016	2020	
[Anonymous], 2015, J HEPATOL, V63, P237, DOI 10.1016/j.jhep.2015.04.006, DOI	2015	11.07	2016	2019	
Younossi ZM, 2016, HEPATOLOGY, V64, P73, DOI 10.1002/hep.28431, DOI	2016	25.63	2017	2021	
EASL, 2016, OBESITY FACTS, V9, P65, DOI 10.1159/000443344, DOI	2016	23.61	2017	2021	
Rinella ME, 2015, JAMA-J AM MED ASSOC, V313, P2263, DOI 10.1001/jama.2015.5370, DOI	2015	8.27	2017	2020	
Singh S, 2015, CLIN GASTROENTEROL H, V13, P643, DOI 10.1016/j.cgh.2014.04.014, DOI	2015	7.85	2017	2020	
Wong RJ, 2015, GASTROENTEROLOGY, V148, P547, DOI 10.1053/j.gastro.2014.11.039, DOI	2015	7.44	2017	2020	
Imajo K, 2016, GASTROENTEROLOGY, V150, P626, DOI 10.1053/j.gastro.2015.11.048, DOI	2016	7.37	2017	2021	
McPherson S, 2015, J HEPATOL, V62, P1148, DOI 10.1016/j.jhep.2014.11.034, DOI	2015	10.98	2018	2020	
McPherson S, 2017, AM J GASTROENTEROL, V112, P740, DOI 10.1038/ajg.2016.453, DOI	2017	7.47	2018	2022	
Dulai PS, 2017, HEPATOLOGY, V65, P1557, DOI 10.1002/hep.29085, DOI	2017	10.82	2019	2022	
Xiao GQ, 2017, HEPATOLOGY, V66, P1486, DOI 10.1002/hep.29302, DOI	2017	8.85	2019	2022	
Hagström H, 2017, J HEPATOL, V67, P1265, DOI 10.1016/j.jhep.2017.07.027, DOI	2017	7.29	2019	2022	
Castagnoli L, 2019, GREEK MEMORIES, V0, PP1, DOI 10.1053/j.gastro.2018.12.036, DOI	2019	8.47	2021	2022	
Berzigotti A, 2021, J HEPATOL, V75, P659, DOI 10.1016/j.jhep.2021.05.025, DOI	2021	14.14	2022	2024	
Davison BA, 2020, J HEPATOL, V73, P1322, DOI 10.1016/j.jhep.2020.06.025, DOI	2020	11.44	2022	2024	
Powell EE, 2021, LANCET, V397, P2212, DOI 10.1016/S0140-6736(20)32511-3, DOI	2021	8.05	2022	2024	

B



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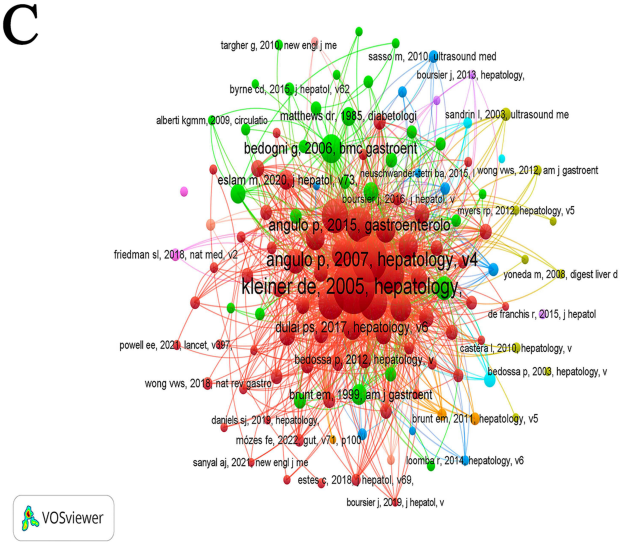

Figure 9 (**A**) Top 25 references with the strongest citation bursts. (**B**) Literature in the field of non-invasive techniques to diagnose and monitor NAFLD with at least 25 citations. (**C**) Analyzing co-citations to identify the most influential articles.

Co-Occurrence Analysis of Keywords

Analyzing keyword co-occurrence serves as a significant method for identifying research hotspots within a specific field. This research utilizes VOSviewer to conduct the keyword co-occurrence analysis. As depicted in Figure 11B, from a total of 2860 keywords, we identified 161 keywords that appeared 10 times or more for further examination. The ten keywords with the highest frequency were: "nafld" (n = 417), "fibrosis" (n = 331), "diagnosis" (n = 236), "non-alcoholic fatty liver disease" (n = 227), "steatohepatitis" (n = 190), "fatty liver disease" (n = 180), "disease" (n = 168), "prevalence" (n = 165), "steatosis" (n = 152), and "transient elastography" (n = 134). These results indicate the continued relevance of non-

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Table 5 Top 10 the Most Cited Literature

Rank	Total Citations	Title	The First Author	Journal	Publication Year
1	340	Design and validation of a histological scoring system for nonalcoholic fatty liver disease[26]	Kleiner, DE	Hepatology	2005
2	265	The NAFLD fibrosis score: A noninvasive system that identifies liver fibrosis in patients with NAFLD[27]	Angulo, P	Hepatology	2007
3	187	Global Epidemiology of Nonalcoholic Fatty Liver Disease-Meta-Analytic Assessment of Prevalence, Incidence, and Outcomes[28]	Younossi, ZM	Hepatology	2016
4	185	Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection[29]	Sterling, RK	Hepatology	2006
5	176	Liver Fibrosis, but No Other Histologic Features, Is Associated With Long-term Outcomes of Patients With Nonalcoholic Fatty Liver Disease[30]	Angulo, P	Gastroenterology	2015
6	176	EASL-EASD-EASO Clinical Practice Guidelines for the Management of Non-Alcoholic Fatty Liver Disease[31]	EASL	Obesity Facts	2016
7	166	The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases[32]	Chalasani, N	Hepatology	2018
8	137	A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C[33]	Wai, CT	Hepatology	2003
9	137	The Fatty Liver Index: a simple and accurate predictor of hepatic steatosis in the general population[34]	Bedogni, G	Bmc Gastroenterol	2006
10	122	Fibrosis Stage Is the Strongest Predictor for Disease-Specific Mortality in NAFLD After Up to 33 Years of Follow-Up[35]	Ekstedt, M	Hepatology	2015

Table 6 Top 10 Keywords in Terms of Publications and Centrality

Rank	Count	Centrality	Year	Keyword	Rank	Centrality	Count	Year	Keyword
1	250	0.04	2014	fibrosis	1	0.31	11	2018	health
2	247	0.01	2014	nafld	2	0.3	43	2015	noninvasive assessment
3	237	0	2014	non-alcoholic fatty liver disease	3	0.25	45	2014	cardiovascular disease
4	214	0.1	2014	diagnosis	4	0.25	15	2014	adipose tissue
5	195	0.04	2014	fatty liver disease	5	0.19	54	2015	hepatocellular carcinoma
6	174	0.02	2014	steatohepatiti	6	0.15	32	2014	population
7	167	0.01	2015	disease	7	0.15	17	2018	feature
8	162	0.06	2014	prevalence	8	0.14	30	2016	advanced fibrosis
9	157	0.05	2014	risk	9	0.14	18	2016	body mass index
10	134	0.02	2014	transient elastography	10	0.14	15	2014	adolescent

invasive diagnostic techniques, particularly transient elastography, in NAFLD research, while also offering valuable insights for future studies.

As illustrated in Figure 11C, the analysis of the average occurrence of keywords in published literature indicates that the color blue signifies keywords that emerged earlier, while yellow denotes those that have come to prominence recently. The figure displays four clusters that reflect a progressive evolution in NAFLD research, transitioning from the pathology of NAFLD diagnosis, diagnostic methods, and lipid metabolism towards themes such as disease regression, associated biomarkers, and the clinical application of non-invasive techniques for both diagnosis and monitoring of NAFLD. This transition suggests that future research should prioritize non-invasive strategies and disease models to enhance the development of innovative diagnostic and therapeutic solutions to mitigate harm to the patient's body.

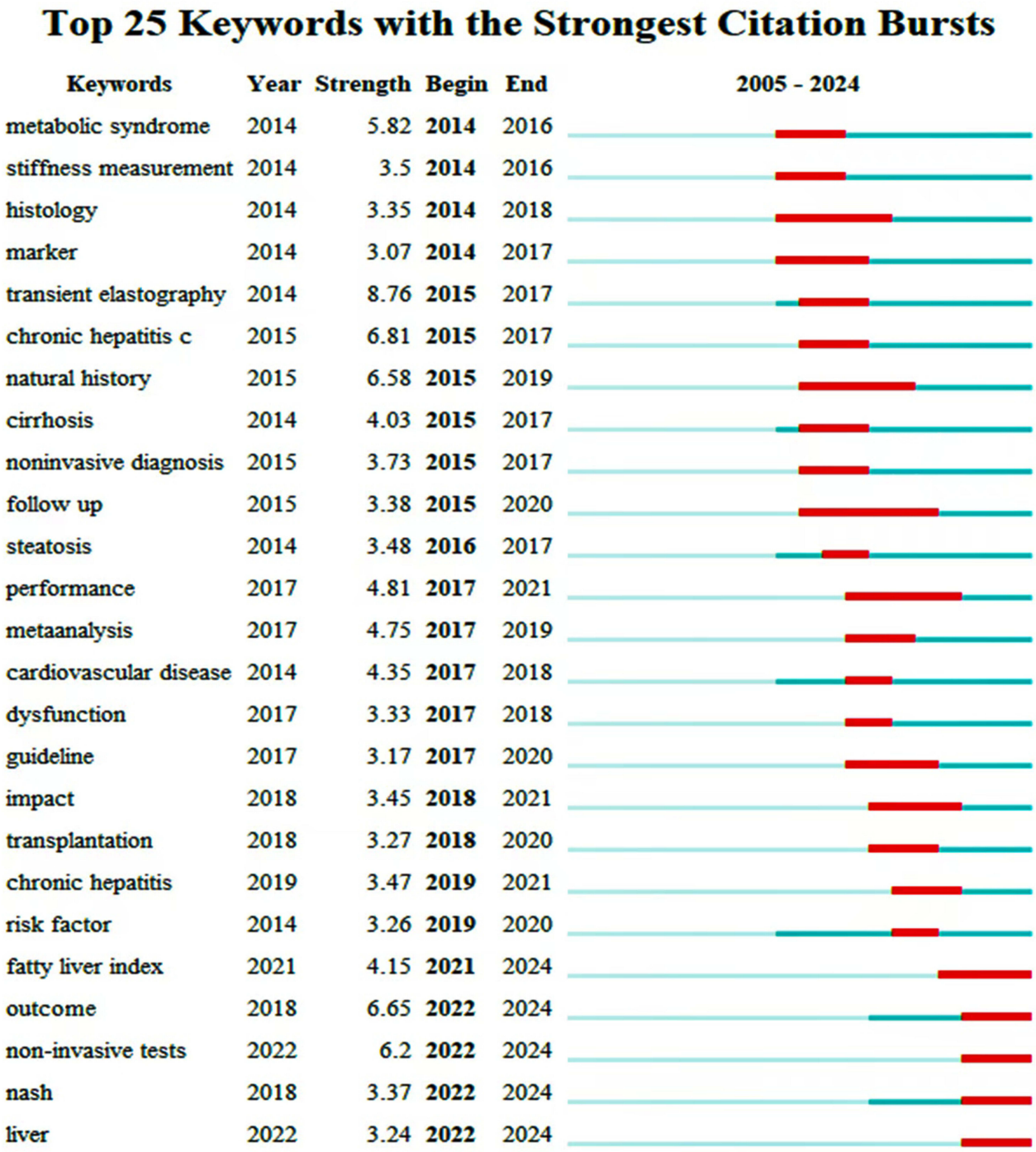

Figure 10 Top 25 keywords with the strongest citation bursts.

Timeline View of Keywords

The timeline graph of keywords was created using CiteSpace software, illustrating the progression of topics and significant research trends within the NAFLD research field from 2005 to 2024. The different colors represent the clustered themes: #0 non-alcoholic fatty liver disease, #1 volatile organic compounds (VOCs), #2 simple noninvasive index, #3 metabolic syndrome, #4 transient elastography, #5 chronic liver disease, #6 mortality, #7 controlled attenuation parameter (CAP), #8 liver disease and #9 marker. The horizontal axis, extending from left to right, represents the

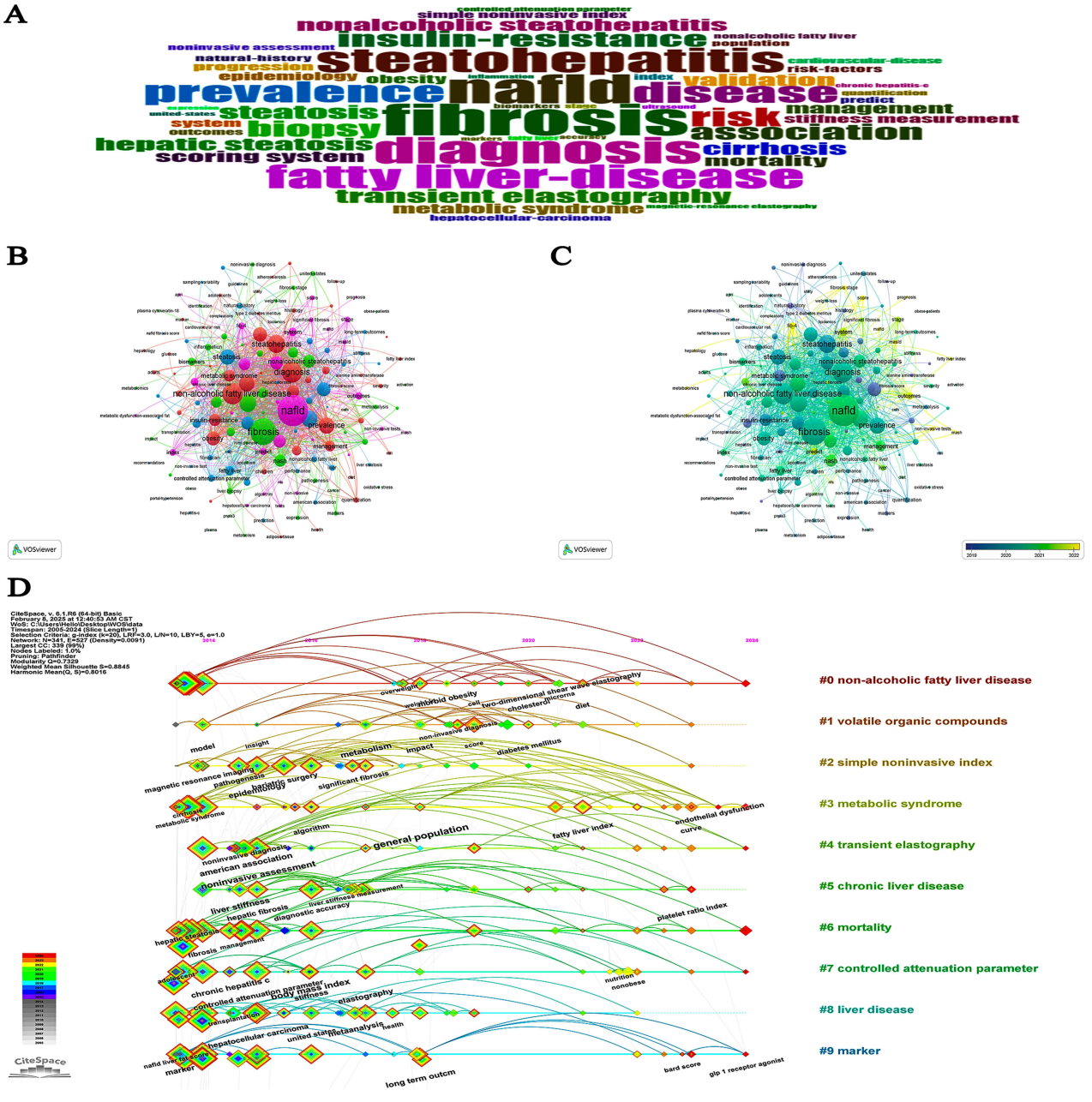

Figure 11 (**A**) Keyword cloud map. (**B**) Keyword analysis based on the VOSviewer visual map. (**C**) Average citation year based on keyword clustering. (**D**) A timeline view of keywords.

development of each keyword over time. Nodes symbolize keywords, with their sizes correlating to the frequency or significance of the keywords. The connecting lines indicate co-occurrence. In Figure 11D, the dynamic landscape of NAFLD research unfolds, which initially focused on the diagnostic criteria and epidemiological studies of NAFLD before delving into a series of non-invasive diagnostic techniques, such as transient elastography. Recent domestic and international research have concentrated on the prognosis, mortality, and biomarkers (eg, VOCs, CAP) associated with NAFLD. These developments highlight the continuous exploration and advancement of researchers in the diagnosis and management of NAFLD.

Analysis of the Evolution of Future Research Themes and Trends

As illustrated in Figure 12A, each rectangle corresponds to a distinct time period, whereas each colored bar represents a specific theme. The dimensions of the bars represent both the frequency of the theme's occurrence and the concentration of the research. Bars of different colors denote various topic categories, and the lines connecting these bars indicate the relationships between different subjects. The evolution of themes portrayed in the figure captures the dynamic changes in NAFLD-related research. A growing cohort of researchers from both domestic and international backgrounds are transitioning their focus from fundamental NAFLD research to its clinical applications, and subsequently to investigations involving particular populations and associated comorbidities.

The diagram illustrates the scope and importance of different themes within the field of liver disease research. Themes are classified into "niche themes", "basic themes", and "motor themes". Niche themes include factors such as risk elements, alanine aminotransferase levels, and follow-up biomarkers, which exhibit low relevance and development density. Conversely, basic themes such as fibrosis and the diagnosis of NAFLD demonstrate high relevance, highlighting their importance in research efforts. Motor themes, which include transient elastography, measurement of stiffness, and non-invasive assessment, reveal a notable development density, indicating their emergence or growth in research focus. In summary, Figure 12B provides valuable insights into the progression and future directions of NAFLD research themes.

Figure 12C presents the trends in subject terms for NAFLD-related research conducted between 2008 and 2024. The figure depicts various terms, with the size of the dots indicating their frequency across different years. The topics range

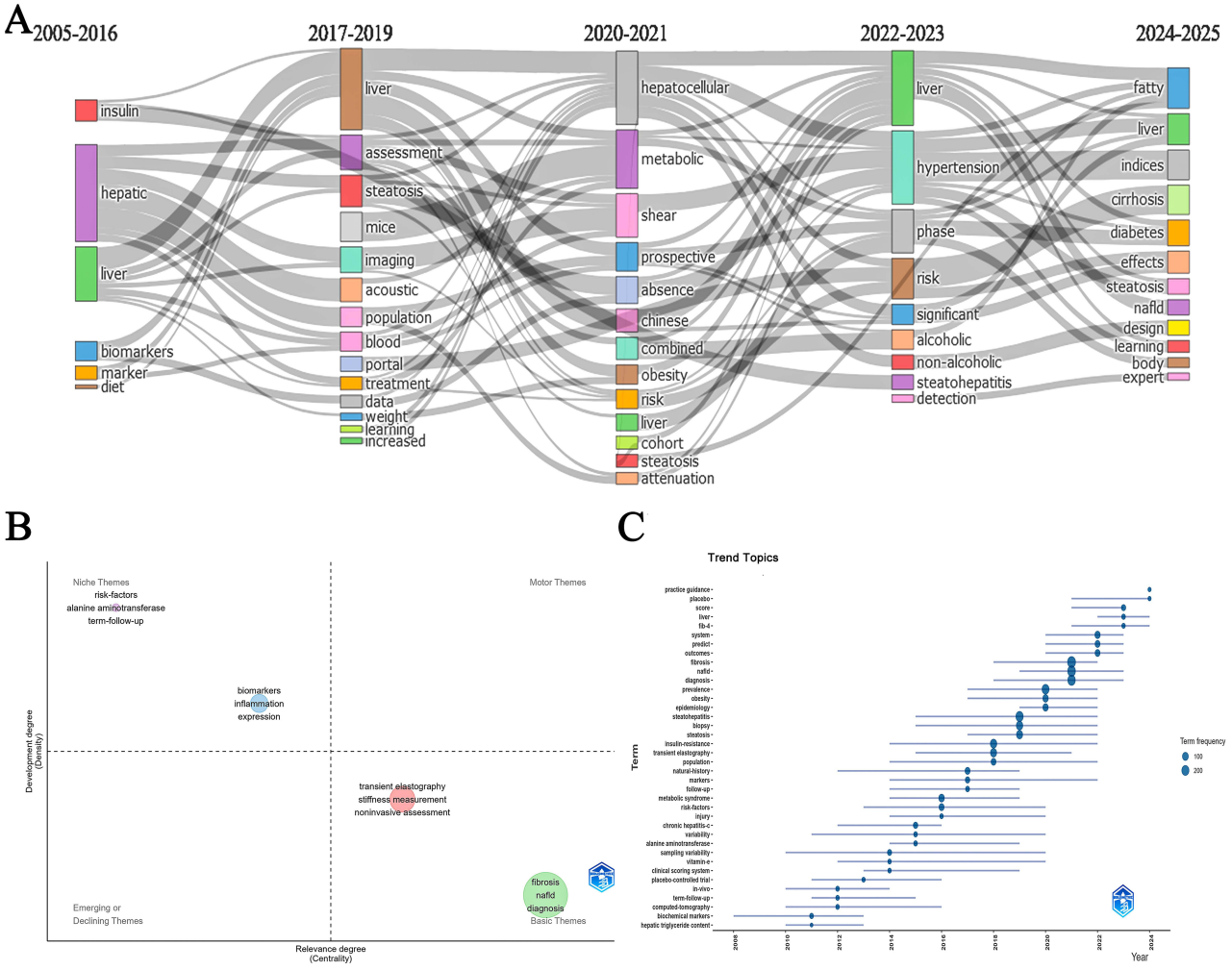

Figure 12 (**A**) Theme evolution: temporal trajectory of NAFLD research. (**B**) Trend analysis of NAFLD research themes. (**C**) Trends in research topics in NAFLD.

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from "practice guidance" to "hepatocellular carcinoma", illustrating the evolving hotspots and trends in NAFLD-related investigations. Notably, terms like "NAFLD diagnosis" and "transient elastography", have shown an increased frequency of occurrence, suggesting that the use of non-invasive techniques for the clinical diagnosis and monitoring of NAFLD progression has gained significant attention from researchers in different countries. This trend highlights the growing focus on non-invasive techniques for diagnosing and tracking NAFLD advancement in clinical settings globally.

Discussion

General Description

This study employed a combination of bibliometric tools to analyze articles published in the core database of WOS from 2005 to 2024 related to non-invasive techniques for the diagnosis and monitoring of NAFLD.[36,37] The aim was to investigate research focal points and anticipate future trends and directions. The findings revealed a significant increase in global publications starting from 2020, peaking in 2023, reflecting the growing interest and potential for future basic research and clinical applications in this field.[38]

The global number of publications in this field has increased steadily, with the United States having the highest number of publications over the past nearly 20 years. Meanwhile, Chinese scholars have also made important contributions to this field, with the total number of published articles accounting for 15.85% of the global total, second only to the United States. The focus of domestic researchers on non-invasive techniques for the diagnosis and monitoring of NAFLD may be mainly attributed to the following reasons: First, with the continuous improvement of the socio-economic level, the quality of life of the domestic population has been significantly improved, but due to unhealthy diets or lifestyles,[39–41] such as smoking, drinking, high-fat and high-sugar diets, etc., the process of obesity is exacerbated, thereby inducing NAFLD.[42–44] In the past 10 years, the prevalence of NAFLD in China has soared from 18% to 29%, which has attracted the widespread attention of domestic scholars.[45]

Excessive social pressure can induce anxiety and insomnia, resulting in shortened nighttime sleep duration and decreased sleep quality.[46] In response to the rapid urbanization and substantial personal, family, and social burdens in developed Chinese cities, scholars have investigated the correlation between sleep duration and NAFLD to enhance clinical interventions for this condition.[47]

Currently, atmospheric pollution has increasingly become a significant global public health issue, drawing widespread attention from countries around the world.[48] Numerous studies have highlighted $PM_{2.5}$, a prominent component of atmospheric pollution, can enter the bloodstream through inhalation exposure when people are exposed to $PM_{2.5}$ environments for a long time, exerting detrimental effects on various organs, including the liver.[49] Although the potential molecular mechanisms of $PM_{2.5}$ on NAFLD have not yet been clarified, cohort studies within Chinese populations have revealed a positive association between $PM_{2.5}$ exposure in living environments and the occurrence and development of NAFLD.[48,49]

The final important reason is the increasing prevalence of NAFLD in the middle-aged and elderly population due to the continuous aging of the domestic population. Furthermore, NAFLD is closely associated with an increased risk of extrahepatic complications, including CVD, T2DM, and chronic kidney disease (CKD).[50–52] These multisystem diseases lead to multimorbidity in elderly individuals, imposing significant economic pressure and a heavy healthcare burden on families and society.[53]

Although China's publication output in this field has steadily increased, its collaboration and citation impact still trail that of the United States. This may be attributed to several factors. Primarily, China's international research partnerships are limited, with a predominant focus on domestic collaborations. Additionally, American scholars maintain significant influence in the academic discourse, particularly through prolific publications in prestigious journals, solidifying the United States' global leadership in the field.[37,38] Furthermore, many recent studies in China have been constrained to cross-section designs, which lack sufficient persuasiveness and clinical applicability.[54,55] There is a notable absence of higher-evidence-level studies, such as randomized controlled trials and large-scale cohort studies.[25]

Among numerous global research institutions, the University of California, San Diego, stands out as a leading entity. Noteworthy publications in Liver International and PLOS ONE contribute to the scholarly discourse, while the Journal of

Hepatology (IF = 26.8) reigns as a preeminent journal in hepatology. Key research areas include "transient elastography", "fibrosis", and "diagnosis". The research trend is transitioning from basic research to clinical applications, emphasizing non-invasive diagnostics, biomarkers, and disease prediction models.

Hot Spots and Frontiers

The burst intensity of keyword citation can be used to identify research hotspots within a field. In this study, "transient elastography" had the highest burst intensity. Given the importance of stage-based management of NAFLD and the limitations of liver biopsy, actively exploring alternatives to liver biopsy has become a research focus.[56–58] Among them, transient elastography plays a crucial role in the early detection and disease monitoring of NAFLD by assessing the degree of liver fibrosis and cirrhosis.[59] Two research teams led by Xiaotao Zhang and Yuan J conducted cross-sectional studies on the adult population in the United States, further confirming the clinical value of transient elastography.[60,61] The burst intensity of "chronic hepatitis C" is also relatively high. There are similarities between chronic hepatitis C (CHC) and NAFLD.[62–64] Both diseases carry the risk of progressing to liver fibrosis and cirrhosis.[65] Therefore, early diagnosis and screening of CHC are equally important.[66] A systematic review on chronic viral hepatitis and metabolic disorders by Chia-Chi Wang et al further confirmed the above-mentioned view.[67]

The keyword "follow-up" had the longest burst duration, lasting from 2015 to 2020. Research by Elena S. George et al[68] indicated that long-term follow-up can track the disease progression of NAFLD in patients. Meanwhile, follow-up can assess the long-term effectiveness of non-invasive diagnostic techniques.[35,69,70] Chinese scholars Zhen-Ya Lu etal[71] conducted an eight-year follow-up study to observe the prevalence and triggering factors of NAFLD in the domestic patient population. The follow-up survey by Wile Balkhed et al[72] is crucial for exploring the natural course of NAFLD and validating the reliability of non-invasive monitoring methods.[73,74]

Keyword burst detection can also be used to identify emerging trends and future research directions. The analysis shows that the research focus in this field has shifted over the years. From 2013 to 2019, the research mainly concentrated on "metabolic syndrome",[75,76] "population",[77,78] "steatohepatitis",[77,79] "alanine aminotransferase level",[80–83] "skeletal muscle",[84] "cardiovascular risk",[85,86] "coronary heart disease",[87,88] "activated protein kinase",[89–91] "nutrition examination survey",[92,93] etc.

In recent years, there has been a gradual transition in research focus from fundamental investigations to clinical applications, specifically in the advancement of non-invasive diagnostic and screening technologies for NAFLD. Scholars globally have implemented diverse strategies for the non-invasive diagnosis and monitoring of NAFLD, including: (1) Utilizing bioinformatics algorithms like machine learning and deep learning to develop and validate early prediction and prognostic models for NAFLD;[94–97] (2) Integrating multi-omics technologies, spanning genomics, metabolomics, transcriptomics, proteomics, and radiomics, to comprehensively elucidate the complex molecular mechanisms underlying NAFLD pathogenesis, which may provide a foundation for the development of novel clinical therapeutics;[98–102] (3) Actively exploring emerging non-invasive biomarkers to evaluate NAFLD progression, enhancing diagnostic precision and reducing reliance on liver biopsy, thereby facilitating early detection and enhancing patient outcomes;[103–106] (4) Implementing AI-driven precision medicine, which refines NAFLD diagnostic models through the analysis of diverse data sources (eg, electronic health records, imaging studies, and pathological data), thereby enhancing diagnostic accuracy and personalization, and providing crucial support for clinical decision-making.[107–110]

Strengths and Limitations

This study systematically combines multi-dimensional bibliometric methods to analyze advancements in non-invasive techniques for NAFLD diagnosis and monitoring over nearly two decades, ensuring broad temporal coverage and comprehensive analysis. It identifies the dominant roles of the United States and China in global research output and demonstrates how international collaborations accelerate technological translation. Clinically, it highlights a clear trend from basic research to AI-driven precision medicine, while pinpointing critical challenges such as the lack of standardized diagnostic thresholds and limited multicenter validation. These findings establish a strategic framework to guide future interdisciplinary investigations in this field.

Furthermore, there are numerous restrictions in this study. First of all, the data used for bibliometric and visual analysis are solely sourced from the WOS core database, without retrieving all the literature in the WOS database. Secondly, during the

retrieval process, the types of literature and languages were restricted, which may lead to a bias in the final analysis results. Finally, the findings presented in this study reflect prevailing perspectives derived from prior literature analysis. Consequently, as future studies emerge, certain conclusions may diverge from evolving empirical evidence. Readers are advised to interpret these results with critical scrutiny.

Conclusion

Our analysis reveals that future research trends concerning the diagnosis and monitoring of NAFLD are likely to evolve towards the clinical application and investigation of non-invasive techniques, including transient elastography, magnetic resonance imaging, the development and validation of predictive models, biomarkers, multi-omics integration, and AI-driven precision medicine.

In summary, although current research indicates that non-invasive techniques cannot fully replace the gold standard of liver biopsy, their advantages remain significant. These techniques are indispensable in the management of NAFLD, MAFLD, and MASLD due to their high diagnostic accuracy, capacity to facilitate early intervention, and ability to dynamically monitor disease progression and therapeutic efficacy. Over the coming years, researchers worldwide are expected to strengthen international collaborations to advance non-invasive techniques, thereby enabling their pivotal role in the diagnosis and treatment of fatty liver diseases.

Data Sharing Statement

The dataset used and/or analyzed during this study is available upon reasonable request from the author of the article.

Ethics Approval

The datasets utilized in this study were obtained from a publicly accessible database. Importantly, our research did not include any experimental procedures involving human or animal subjects. Therefore, ethics board approval was not necessary.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work. All authors have read and agreed to the published version of the manuscript.

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Disclosure

The authors affirm that the research was carried out without any commercial or financial affiliations that could be seen as a potential conflict of interest.

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